Extra-Lymphatic Filariasis: A Study of Three Interesting Cases

INTRODUCTION
Filariasis is a chronic disabling parasitic disease that causes a major public health problem in tropical countries like India. *Wuchereria bancrofti* is associated with almost 99.4% of cases. Filariasis not only affects the structure and function of lymphatic vessels but is also associated with extra-lymphatic pathology and diseases. Lymphatic filariasis is commonly found throughout the tropics and subtropics. While lymph nodes are the common sites, unusual sites include the breast, spleen, subcutaneous tissue, thyroid, bone marrow, urinary tract, sputum, bronchial washing, pleural and pericardial fluid. Patients from endemic areas presenting with swelling should be evaluated for filariasis. Here in present case series, the authors discussed three cases: filariasis of the breast with fibroadenoma, soft-tissue nodule, and splenic lesions, due to their extreme rarity and unusual sites. In the first case, 20 years old female patient presented with a lump in the left breast. The complete blood cell (CBC) revealed eosinophilia, but peripheral smears did not show the presence of microfilariae. On Fine Needle Aspiration Cytology (FNAC), smears showed *Wuchereria bancrofti* microfilaria in the background of fibroadenoma. The patient was treated with Diethylcarbamazine (DEC) for 21 days. Repeat CBC revealed a decrease in the absolute eosinophil count. Lumpectomy for fibroadenoma was performed, which showed fragments (dead) of the microfilarial parasite. The association of filariasis with fibroadenoma is possibly due to pre-existing subclinical filariasis when the neoplasm developed, as the patient hails from an endemic area. Filariasis presenting as a soft-tissue nodule is an uncommon incidence. In the second case discussed here, 30 years old female patient had soft-tissue swelling over the left elbow. Peripheral smear only revealed eosinophilia without any parasites. On FNAC, smears showed *Wuchereria bancrofti* microfilaria, along with lymphoid cells and a few eosinophils. The swelling subsided with DEC treatment, and repeat CBC showed a decrease in the absolute eosinophil count. The third case discussed here, involved an unknown 35 years old male, who was brought dead to the hospital. No clinical details were available. On autopsy, the spleen showed multiple white patches, ranging in size from 0.2 to 0.5 cm in diameter. All other organs were unremarkable. Microscopy showed many granulomas and numerous dead fragmented microfilariae. It was a case of isolated splenic filariasis, which is a rarely diagnosed entity. These unique cases will raise awareness of diagnosing and instituting proper therapy.

CASE SERIES

Case-1
A 20-year-old female patient presented with a gradually increasing lump in the left breast since eight months. During the history-taking, it was revealed that the patient had a history of moderate-grade fever without chills since two months. On clinical examination, a well-defined, non-tender, freely mobile lump measuring 2.5×2.5 cm was palpable in the upper and outer quadrant of the breast. There was no evidence of lymphadenopathy or hepatosplenomegaly. The CBC revealed mild eosinophilia with an absolute eosinophil count of 720/cmm (0 to 500/cmm). Peripheral smears did not show the presence of microfilariae. Investigation of FNAC of the breast lump showed monolayered sheets and clusters of benign ductal epithelial cells, suggesting a fibroadenoma [Table/Fig-1a]. The smears also showed a few sheathed microfilariae with nuclei-free tail tips [Table/Fig-1b]. A diagnosis of fibroadenoma with filarial infestation by *Wuchereria bancrofti* was made. The patient was treated with DEC (dosage: 6mg/kg) for 21 days. Repeat CBC revealed a decrease in the absolute eosinophil count to 170/cmm. Subsequently, the patient underwent lumpectomy. Grossly, the lump had a grey-white myxoid appearance on the cut surface with slit-like spaces [Table/Fig-1c]. Histopathology showed features of fibroadenoma with the presence of fragments of microfilarial parasites in the interlobular stroma, confirming the diagnosis of fibroadenoma with the presence of microfilarial parasites [Table/Fig-1d]. Sparse lymphocytic infiltrate with occasional eosinophils was observed. However, a granulomatous...
reaction was not seen. Hence, the diagnosis of Bancroftian filariasis of the breast with fibroadenoma was established. After the lumpectomy, the symptoms resolved.

Case 2
A 30-year-old female patient presented with swelling in the left elbow for the past two years. The swelling was not associated with pain, tingling, or numbness. There was no history of trauma, fever, cough, cold, weight loss, or loss of appetite. The patient had no past history of tuberculosis or contact with tuberculosis. There were no known medical conditions such as hypertension, diabetes, or bronchial asthma.

CBC revealed mild eosinophilia (absolute count 600/cmm), and no parasites were seen on peripheral smear. Ultrasound showed a hypoechoic lesion in the anterolateral aspect of the left elbow. The differential diagnosis based on ultrasound was a nerve sheath tumour. On investigation, FNAC of the swelling revealed a polymorphic population of lymphoid cells mixed with a few eosinophils. Additionally, occasional sheathed microfilaria larvae with nuclei-free tail tips were observed, along with epithelioid granulomas. There was no evidence of caseation necrosis. The diagnosis of a granulomatous lesion (Wuchereria bancrofti) was made [Table/Fig-2]. The patient was treated with DEC (dosage: 6 mg/kg) for 21 days, and the swelling subsided. Repeat CBC showed an absolute eosinophil count of 200/cumm.

Case 3
A 35-year-old unknown male was brought dead to the hospital, and an autopsy was performed. The spleen showed multiple, white patches ranging in size from 0.2 to 0.5 cm in diameter [Table/Fig-3a]. On autopsy, all other organs appeared unremarkable grossly. Microscopic examination revealed numerous granulomas [Table/Fig-3b] and fragmented microfilariae in a deceased state [Table/Fig-3c]. Since the patient's identity was unknown and there were no available clinical details, only the spleen exhibited the mentioned histopathological findings. The other organs were unremarkable both grossly and microscopically. Therefore, the authors consider splenic filariasis to be an incidental finding encountered during post-mortem histopathological examination.

DISCUSSION
According to the World Health Organization (WHO), Filariasis is identified as a significant global health problem that causes permanent and long-term disability [7]. Lymphatic filariasis is found in heavily infected states such as Uttar Pradesh, Bihar, Jharkhand, Andhra Pradesh, Orissa, Tamil Nadu, Kerala, and Gujarat. In India, Wuchereria bancrofti and Brugia malayi are mainly responsible for filariasis. Morphologically, both have sheathed microfilariae. The tail tip of Wuchereria bancrofti is free of nuclei, while that of Brugia malayi shows terminal two nuclei. In endemic countries, Wuchereria bancrofti is responsible for 98% of infections [7].

The microfilariae are released into the peripheral circulation, while the adult worm resides in the lymphatics of the hosts [6]. Extravasation of the larval form occurs due to lympho-vascular obstruction, potentially reaching the tissue space [8]. The lymphatics of the splanchnic cord, epididymis, mammary glands, lower limbs, and retroperitoneal tissue are most frequently affected [6]. In this case series, first two cases did not show microfilariae on peripheral smear but showed filariasis on FNAC of the breast and soft tissue. Thus, filariasis can exist without microfilaremia, as reported by many authors [4,9]. Both cases showed eosinophilia on CBC. Yenkeshwar PN et al., in their report of 22 cases of microfilariae in FNA from various sites, similarly found eosinophilia in five cases [6].

Filariasis should be considered as a differential diagnosis in patients presenting with subcutaneous nodules in filarial endemic zones, as seen in the present two FNAC cases who hailed from Uttar Pradesh. Eosinophilia on peripheral smear and cytology provide supporting findings for the diagnosis of filariasis. The morphology of microfilariae on FNAC smears helps identify the species. In these cases, both were morphologically Wuchereria bancrofti. FNAC diagnosis of microfilariae is important for early diagnosis and medical treatment, which avoids further surgical intervention [6].
In breast filariasis, lymphangitis and fibrosis are caused by lymphatic obstruction. It may mimic malignancy, as it can present with enlargement of axillary nodes and hyperemia of the overlying skin, resulting in a peau d’orange appearance [4,10,11]. Rarely, microfilariae coexist with neoplastic lesions. Yenkhswana PN et al., found microfilariae in three cases of the breast, one of which was associated with infiltrating duct carcinoma [6]. Pantola C et al., in their series of seven cases, reported microfilariae coexisting with six malignant lesions, including one case of breast adenocarcinoma, and one benign lesion, pleomorphic adenoma of the parotid gland [12]. Gupta N and Chawla A reported a case of filariasis of the breast, clinically masquerading as fibroadenoma [11]. Filariasis against background of fibroadenoma is an extremely rare association, which was observed in one of the presently discussed cases. The association of filariasis with fibroadenoma is possibly because of pre-existing subclinical filariasis, as the patient hails from an endemic area (UP) [4]. Some authors have suggested increased vascularity associated with lesions as a cause for the presence of microfilaria in neoplasms [12]. The present findings correlate with similar reported literature [Table/Fig-4a].

Skin and soft-tissue swelling, breast, thyroid, salivary glands, cervicovaginal smears, ovarian cysts, effusion fluids, urine, bronchial, laryngeal, and pharyngeal brushings are infrequent sites where extranodal filariasis has been documented [6]. In studies conducted by Yenkhswana PN et al., and Mishra R et al., soft tissue and breast were common sites [6,13]. People in endemic areas get infected early in life and develop microfilaraemia between 15-20 years of age [13]. Several studies of subcutaneous swelling showing microfilaria have been tabulated, which correlate with the present findings [Table/Fig-4b].

In the third case, autopsy showed isolated splenic filariasis with multiple non-necrotising granulomatous lesions on histopathology. Although filariasis is ubiquitous and frequently present in India, it rarely results in splenic symptoms as observed in here. Dhayagude [14] and Amin BM documented that filariasis can produce lesions in the spleen with or without eosinophilia and concluded that it can be an incidental finding [14]. Hence, in cases of multiple splenic granulomatous lesions, the differential diagnosis of splenic filariasis should be considered [Table/Fig-4c] [1,3,14,22].

Table/Fig-4a-c: Comparison of the current study with similar reported literature in last 5 years [1,3,15-22]: a: Breast filariasis; b: Subcutaneous swelling; c: Splenic filariasis.

The diagnosis of filariasis is made by demonstrating microfilaria in stained or unstained blood films and detecting filarial antigen at low levels of microfilaria. The majority of affected individuals remain asymptomatic, with continued disease transmission in endemic areas [5].

CONCLUSION(S)

In a patient coming from endemic areas of filariasis with a lump at any site, one should keep the possibility of filariasis in mind. Careful screening of cytology slides for microfilariae should be done. Fine-needle aspiration cytology (FNAC) of these nodules can be really helpful in such cases, and an awareness and active search for an adult worm or microfilaria should be undertaken for an accurate diagnosis. When considering a case of multiple symptomatic/ asymptomatic splenic granulomatous lesions, the differential diagnosis of splenic filariasis should be taken into account.

REFERENCES

PARTICULARS OF CONTRIBUTORS:
1. Resident, Department of Pathology, Rajiv Gandhi Medical College and Chhatrapati Shivaji Maharaj Hospital, Kalwa, Thane, Maharashtra, India.
2. Assistant Professor, Department of Pathology, Rajiv Gandhi Medical College and Chhatrapati Shivaji Maharaj Hospital, Kalwa, Thane, Maharashtra, India.
3. Professor (Additional), Department of Pathology, Rajiv Gandhi Medical College and Chhatrapati Shivaji Maharaj Hospital, Kalwa, Thane, Maharashtra, India.
4. Professor (Additional), Department of Pathology, Rajiv Gandhi Medical College and Chhatrapati Shivaji Maharaj Hospital, Kalwa, Thane, Maharashtra, India.
5. Associate Professor, Department of Pathology, Rajiv Gandhi Medical College and Chhatrapati Shivaji Maharaj Hospital, Kalwa, Thane, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Yogesh Vishnu Badak, Rajiv Gandhi Medical College and Chhatrapati Shivaji Maharaj Hospital, Ground Floor, 32(E), Thane, Maharashtra, India.
E-mail: yogesh.v.badak@gmail.com

AUTHOR DECLARATION:
• Financial or Other Competing Interests: None
• Was informed consent obtained from the subjects involved in the study? Yes
• For any images presented appropriate consent has been obtained from the subjects. Yes

PLAGIARISM CHECKING METHODS:

ETYMOLOGY:
Author Origin

EMENDATIONS: 7

Date of Submission: May 15, 2023
Date of Peer Review: Jul 09, 2023
Date of Acceptance: Oct 19, 2023
Date of Publishing: Apr 01, 2024